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# Minimally Invasive Procedure versus Conventional Redo Sternotomy for Mitral Valve Surgery in Patients with Previous Cardiac Surgery: A Systematic Review and Meta-Analysis

Muhammad Ali Tariq, M.B.B.S.<sup>1</sup>, Minhail Khalid Malik, M.B.B.S.<sup>1</sup>, Qazi Shurjeel Uddin, M.B.B.S.<sup>2</sup>, Zahabia Altaf, M.B.B.S.<sup>2</sup>, Mariam Zafar, M.B.B.S.<sup>2</sup>

<sup>1</sup>Department of Surgery, Dow University Hospital, Dow University of Health Sciences; <sup>2</sup>Department of Surgery, Dow Medical College, Dow University of Health Sciences, Karachi, Pakistan

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#### **Corresponding author**

Muhammad Ali Tariq Tel 92-0312-2319607 Fax 92-342-88454 E-mail MUHAMMAD.TARIQ16@dimc. duhs.edu.pk ORCID https://orcid.org/0000-0003-1108-0731 **Background:** The heightened morbidity and mortality associated with repeat cardiac surgery are well documented. Redo median sternotomy (MS) and minimally invasive valve surgery are options for patients with prior cardiac surgery who require mitral valve surgery (MVS). We conducted a systematic review and meta-analysis comparing the outcomes of redo MS and minimally invasive MVS (MIMVS) in this population.

**Methods:** We searched PubMed, EMBASE, and Scopus for studies comparing outcomes of redo MS and MIMVS for MVS. To calculate risk ratios (RRs) for binary outcomes and weighted mean differences (MDs) for continuous data, we employed a random-effects model.

**Results:** We included 12 retrospective observational studies, comprising 4157 participants (675 for MIMVS; 3482 for redo MS). Reductions in mortality (RR, 0.54; 95% confidence interval [CI], 0.37–0.80), length of hospital stay (MD, -4.23; 95% CI, -5.77 to -2.68), length of intensive care unit (ICU) stay (MD, -2.02; 95% CI, -3.17 to -0.88), and new-onset acute kidney injury (AKI) risk (odds ratio, 0.34; 95% CI, 0.19 to 0.61) were statistically significant and favored MIMVS (p<0.05). No significant differences were observed in aortic cross-clamp time, cardiopulmonary bypass time, or risk of perioperative stroke, new-onset atrial fibrillation, surgical site infection, or reoperation for bleeding (p>0.05).

**Conclusion:** The current literature, which primarily consists of retrospective comparisons, underscores certain benefits of MIMVS over redo MS. These include decreased mortality, shorter hospital and ICU stays, and reduced AKI risk. Given the lack of high-quality evidence, prospective randomized control trials with adequate power are necessary to investigate long-term outcomes.

**Keywords:** Meta-analysis, Mitral valve, Minimally invasive surgical procedures, Reoperation, Sternotomy, Thoracotomy

## Introduction

Over the past decade, the frequency of redo valve surgery has surged [1]. Within 10 years, nearly 35% of patients with bioprosthetic valves will need to undergo redo surgery [2]. The number of patients requiring this type of surgery is expected to rise in the future, primarily due to degenerated bioprosthetic mitral valves, failed mitral valve annuloplasty, and infective endocarditis. Reoperative valvular surgery carries a comparatively high perioperative mortality rate, up to 3 times that of primary surgery [3].

Median sternotomy (MS) is considered the gold standard for multiple cardiovascular procedures and is the most frequently used surgical approach for repeat valvular surgery [4]. However, repeat MS is a high-risk procedure that often presents challenges. These include increased bleeding, potential injury to vital mediastinal structures, poor access due to dense adhesion, and extended operative time [5]. A minimally invasive surgical approach involving right anterolateral mini-thoracotomy is a viable alternative that

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could mitigate the risks associated with redo-MS. This approach is often associated with a quicker return to daily routines and increased patient satisfaction regarding cosmetic results, which are among the most consistently reported benefits of this method [6]. However, concerns about extended cross-clamp time and prolonged operative times, which could adversely affect surgical outcomes, along with a steep learning curve have hindered its wide-spread adoption in this patient subset [7].

Despite the purported advantages of a minimally invasive approach, no consensus yet exists on the optimal surgical approach for mitral valve operations in patients who have previously undergone cardiac surgery. Most evidence supporting the minimally invasive approach comes from observational and propensity-matched cohorts, with no data from randomized controlled trials. The objective of this study was to conduct a comparative analysis of the outcomes of minimally invasive mini-thoracotomy versus redo MS. By doing so, we aimed to identify the superior surgical approach for mitral valve surgery in patients with a history of conventional sternotomy for cardiac surgery.

## **Methods**

### Protocol and registration

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. The protocol was prospectively registered in the PROSPERO register of systematic reviews (CRD42022359204). The methods of analysis, outcome measures, and inclusion criteria were predetermined and documented in the protocol. We employed the PICOS (patient, intervention, comparison, outcome, and study design) framework to structure our search strategy. Ethical approval was not required because we exclusively analyzed data from previously published studies, for which the primary investigators had already obtained informed consent.

### Literature search

Two authors independently performed a comprehensive literature search of several electronic databases, including PubMed, Scopus, and Embase, from their inception to January 2023. No restrictions were made regarding date, language, or study design. The detailed search strategy was formulated using relevant keywords and Medical Subject Heading (MeSH) terms, combined with the Boolean operators AND/OR. Search terms included variations of "thoracotomy," "mitral valve," "mini thoracotomy," "redo mitral valve," redo valve," "reoperative mitral valve," "thoracotomy," and "median sternotomy." In addition, we manually searched selected articles and reviews to identify relevant studies. First, duplicate articles were removed, and a title and abstract screening was conducted for all retrieved studies. Subsequently, the full text of all relevant articles was obtained, and articles were selected for inclusion based on the eligibility criteria.

### Study selection: eligibility criteria

The eligibility criteria were established based on the PI-COS principles. The population included adult patients (over 18 years old) with mitral valve disease who required surgery and had a history of at least 1 previous cardiac surgical procedure via MS. The intervention involved minimally invasive mitral valve surgery (MIMVS) via right mini-thoracotomy, which could be performed through port-access or keyhole methods, with either direct visualization or camera assistance through lateral, parasternal, or xiphoid approaches. The comparator was conventional repeat MS. The outcomes included studies that reported data on at least 1 of the predetermined outcomes. The study design encompassed randomized and nonrandomized comparative studies. Studies were excluded if they met any of the following criteria: (1) they were duplicate publications, had overlapping patients, or were subgroup analyses of a main study; (2) they were abstracts, expert opinions, letters to the editor, brief reports, case reports, case series, conference presentations, or editorials; (3) the outcomes of interest were not clearly reported, or it was impossible to extract or calculate them from the published results; (4) they reported combined outcome data for any other valvular procedure, such as tricuspid or aortic valve surgery, along with mitral valve surgery; or (5) they utilized robotic telemanipulation or approaches such as the Da Vinci robot.

### Study outcomes

The primary outcomes of interest for the study were operative mortality (defined as death within 30 days post-operation or during the hospital stay), perioperative stroke, reoperation for bleeding, and the durations of hospitalization and intensive care unit (ICU) admission. Secondary outcomes encompassed the incidence of postoperative surgical site infection, the incidence of acute kidney injury (AKI) requiring dialysis, new-onset atrial fibrillation, crossclamp time, cardiopulmonary bypass time, and blood loss.

#### Data extraction and quality assessment

Two independent investigators were responsible for extracting the following data from studies that satisfied the inclusion criteria: name of the first author, year of publication, country in which the study was conducted, sample size, average patient age, sex of the patients (male or female), previous surgical procedures, concurrent procedures, preoperative characteristics, clamping technique used, method of myocardial protection, study outcomes, and source of funding. Any discrepancies were resolved through consensus. Two authors independently assessed the quality of the included studies. If any discrepancies arose, a third author was consulted. The methodological quality of the studies that met the inclusion criteria was evaluated by 2 authors using the Joanna Briggs Institute Critical Appraisal Checklist. In the event of any disagreement, a third reviewer would be called upon to resolve the issue. This tool was used to evaluate studies based on 11 items, with a maximum possible score of 11 for each study. If the answer to an item was affirmative, the item was assigned a score of 1. If the answer was negative, unclear, or not applicable, the item was given a score of 0.

#### Statistical analysis

Meta-analysis was performed using Stata ver. 17.0 (Stata Corp., College Station, TX, USA). For dichotomous outcomes, risk ratios (RRs) with 95% confidence intervals (CIs) were computed, while for continuous data, weighted mean differences (MD) with corresponding 95% CIs were calculated. The data were pooled using the restricted maximum likelihood random effects model. The chi-square  $(\gamma^2)$ test was employed to assess statistical heterogeneity, with significance considered to be indicated by p-values less than 0.10. The Higgins  $I^2$  statistic was used to estimate the magnitude of the heterogeneity. A high level of heterogeneity was indicated by an I<sup>2</sup> value greater than 75%, a moderate level by an I<sup>2</sup> value between 25% and 75%, and a low level by an I<sup>2</sup> value less than 25%. To identify potential publication bias, we examined funnel plots for asymmetry and applied the Egger regression asymmetry test, considering a p-value less than 0.10 as indicative of publication bias, but only for outcomes with at least 10 studies. For all other analyses, a 2-tailed p-value of less than 0.05 was considered to indicate statistical significance.

## Results

### Study selection

The initial search of the electronic databases yielded 456 citations. Once duplicates were removed, 305 citations remained. A preliminary screening was then conducted based on the title and abstract of each citation, which led to the selection of 61 articles for full-text evaluation based on eligibility criteria. Ultimately, 12 articles, encompassing 4,157 participants, met the criteria and were deemed suitable for inclusion in this meta-analysis [8-19]. The full selection process for the relevant studies is illustrated in Fig. 1.

#### Study characteristics and quality assessment

The 12 studies included in this analysis, published between 2002 and 2021, were all retrospective cohort studies. They represent a total sample size of 4,157 patients, with 675 participants in the minimally invasive group and 3,482 in the redo MS group. The average age of the patients in the minimally invasive group was 62.9±7.28 years, while that of those in the redo sternotomy group was  $60.6\pm5.95$ years. Of the total participants, 1,984 (48.6%) were female and 2,097 (51.4%) were male. However, 1 study did not provide a breakdown of patients by sex, but instead only indicated the total number of participants. Of the 12 studies, 5 were conducted in the United States, 2 each in Canada and South Korea, and 1 each in Japan, China, and Germany. Other baseline characteristics of the patients in each group are highlighted in Table 1. All of the studies were deemed to be of high quality, but as all were retrospective in nature, biases inherent to this type of study remained. More specifically, in terms of patient selection and comparability, all studies were considered high quality. However, only 2 (those by Patel et al. [16] and Losenno et al. [14]) employed strategies to address confounding factors. Details of previous operations, preoperative patient characteristics, and concomitant surgical procedures are presented in Table 2. Only 4 participants (0.43%) in the minimally invasive group underwent conversion to sternotomy. Concomitant procedures were performed in 69.8% of patients (17.2% in the MIMVS and 77.9% in the redo MS group). The most common procedure was ablation in the MIMVS arm (42.4%) and coronary artery bypass grafting among those undergoing redo MS (35.2%).



**Fig. 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flow diagram summarizing the process used to select relevant clinical studies.

### Synthesis of results

### **Primary outcomes**

#### **Operative mortality**

Eleven studies, involving 4,058 participants (663 for MIMVS and 3395 for redo MS), compared the mortality rates between these surgical approaches. The reported mortality rate was 4.52% in the minimally invasive group and 7.45% in the sternotomy group. A pooled analysis revealed a significantly reduced risk of mortality in patients who underwent mitral valve surgery via the minimally invasive thoracotomy approach, compared to those who underwent redo sternotomy (RR, 0.54; 95% CI, 0.37 to 0.80; p<0.001;  $I^2=0.00$ ) (Fig. 2).

#### Duration of hospital stay

Ten studies, involving 1,300 participants (498 for MIM-VS and 802 for redo MS), reported on the length of hospital stays in days. We noted a significantly shorter duration of hospital stays for patients who underwent the minimally invasive approach (MD, -4.23; 95% CI, -5.77 to -2.68; p<0.001; I<sup>2</sup>=42.5%) (Fig. 3).

#### Perioperative stroke

Ten studies, with a total of 3,970 participants (615 for MIMVS and 3,355 for redo MS), evaluated the incidence of stroke between these surgical approaches. The reported stroke rate was 4.55% in the minimally invasive group and

6.49% in the sternotomy group. A pooled analysis revealed no significant difference in the risk of stroke between the 2 methods (RR, 0.84; 95% CI, 0.51 to 1.39; p=0.49;  $I^2=17.8\%$ ) (Fig. 4).

#### Duration of ICU stay

Eight studies, involving 833 participants (341 for MIM-VS and 492 for redo MS), reported on the length of ICU stays in days. We noted a significantly shorter hospital stay duration for patients who underwent the minimally invasive thoracotomy approach (MD, -2.02; 95% CI, -3.17 to -0.88; p<0.001; I<sup>2</sup>=81.4%) (Fig. 5).

#### Secondary outcomes

#### AKI requiring dialysis

Five studies, including 790 participants (334 for MIMVS and 456 for redo MS), provided data on the new onset of AKI requiring dialysis. The reported rate in the minimally invasive group was 3.77%, compared to 13.37% in the sternotomy group. A pooled analysis revealed a significant reduction in the risk of AKI associated with the minimally invasive thoracotomy approach (RR, 0.34; 95% CI, 0.19 to 0.61; p<0.001;  $I^2$ =0.0%) (Fig. 6A).

#### New-onset atrial fibrillation

Four studies, involving 536 participants (147 for MIMVS and 389 for redo MS), reported on the new onset of atrial fibrillation. The reported rate of this condition was 8.84%

JBI critical

Longterm

CKD

COPD

fibrillation Atrial

Diabetes mellitus

Sex (male/female)

Mean age (Yr)

Treatment size

Study

duration Study

Country

Author

Table 1. Baseline characteristics of included studies

IOUNNY	COULINY	di mati an		10	2	~				)	5								CLINCAL
		auration	nesign	MIMVS	rMS	MIMVS	rMS	MIMVS	rMS	MIMVS	rMS	MIMVS	rMS	MIMVS	rMS	MIMVS	rMS f	glow-up	appraisal
Burfeind et al.	USA	1996–2001	Retrospect-	97	155	63.0	58.0	53/44	42/113	ı	ı	ı	I	,	ı	,	ı	Υ	7
[8] (2002)			ive																
Bolotin et al.	USA	January 1996–	Retrospect-	38	38	68.0	63.0	ΝA	٩Z	ī		ı		ī	,	ī		Υ	7
[9] (2004)		June 2003	ive																
Svensson et al.	USA	January 1993–	Retrospect-	80	2,444	63.0	64.0	57/23	1,337/1,107	10	444	18	751	14	634	14	247	ΝA	7
[10] (2007)		January 2004	ive																
Kim et al. [11]	South	September 2007-	Retrospect-	22	13	46.0	45.0	4/18	5/8	-	ŝ	ı	ı	ı	ı	ı		1.6 mo	10
(2012)	Korea	December 2010	ive																
Hiraoka et al.	Japan	January 2006–	Retrospect-	10	27	68.0	62.9	5/5	9/18	Ŋ	6	ī	ı	3	11	ī		Ν	7
[12] (2013)		September 2011	ive																
Vallabhajosyula	USA	1988-2001	Retrospect-	67	220	64.0	61.0	32/35	99/121	6	38	28	66	ı	ı	ı	ī	ΝA	7
et al. [13] (2015	0		ive																
Losenno et al.	Canada	September 2000–	Retrospect-	40	92	68.0	62.0	28/12	38/54	11	14	6	16	16	19	ŝ	4	0 mo	6
[14] (2016)		August 2014	ive PSM																
Ghoneim et al.	Canada	July 2009-	Retrospect-	12	9	67.0	68.5	11/1	5/1	-	С	ı	ı	ŝ	2	2	3	1.6 yr	6
[15] (2016)		February 2015	ive																
Patel et al.	NSA	January 2011–	Retrospect-	06	166	70.4	62.2	54/36	77/89	37	45	ı		22	62	4	4	ΥA	10
[16] (2019)		December 2017	ive PSM																
Zhang et al.	China	January 2006–	Retrospect-	30	50	60.7	60.2	18/12	33/17	9	2	21	13	$\sim$	2	ı		6 mo	10
[17] (2020)		January 2019	ive																
Monsefi et al.	Germany	2017-2020	Retrospect-	27	53	66.0	65.0	13/14	25/28	9	14	ı	ı	ŝ	9	9	15	1 yr	6
[19] (2022)			ive																
Kwon et al.	South	January 2002–July	Retrospect-	162	218	51.5	55.1	59/103	93/125	19	28	81	120	5	10	4	14	5.7 yr	6
[18] (2022)	Korea	2018	ive																
MIMVS, minimall PSM, propensity s	y invasive m core match	nitral valve surgery; r ing.	MS, redo me	edian ste	rnotomy	; copd,	chronic	c obstructi	ve pulmonary o	lisease; (	CKD, chr	onic kid	ney dise	ase; JBI, J	Joanna E	triggs Ins	titute; N	IA, not ap	plicable;

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	Preoperative patier	nt characteristics	Conversion	Concon	nitant surgery	Previons	surgery
Author	MIMVS	rMS	to sternotomy	MIMVS	rMS	MIMVS	rMS
Burfeind et al. [8] (2002)	LVEF (45%±9%), mean NYHA (3.4)	LVEF (54%±13%), mean NYHA (3.5)	NR	NR	NR	MVS (60)	MVS (83)
Bolotin et al. [9] (2004)	LVEF (46%±12%), mean NYHA (2.7)	LVEF (55%±11%), mean NYHA (2.6)	0	NR	NR	NR	NR
Svensson et al. [10] (2007)	NR	NR	NR	CABG (1), TVr (12), TVR (0)	AVR (724), CABG (955), TVr (671), TVR (46)	MVS (32), AVR (13), CABG (53)	MVS (1134), AVR (456), CABG (674)
Kim et al. [11] (2012)	LVEF (61%±9%)	LVEF (45%±16%)	ZR	NR	NR	MVP (59), MVR (9), MVR+TVP/AVR (9), MVP+TVP (5), other (18)	MVP (46), MVP+TVP (8), MVR (8), MVR+TVP/AVR (8), CABG (8), AVR (8), other (22)
Hiraoka et al. [12] (2013)	LVEF (47%±19%), mean NYHA (1.3±0.5), EuroSCORE (4.8±2.0)	LVEF (64±9), mean NYHA (1.3±0.7), EuroSCORE (3.8±2.4)	NR	NR	NR	MVP (4), CABG (3), rMVR (1), AVR (1)	MVP (9), MVR (5), AVR (3), rMVR (1), other (8)
Vallabhajosyula et al. [13] (2015)	LVEF (54%±12%), NYHA >2 (63%)	LVEF (54%±17%), NYHA >2 (69%)	-	TVR (9), ablation (1) ASD/PFO (4)	TVR (26), ablation (22) ASD/PFO (11)	MVP (78), MVR (19), MVP+MVR (3)	MVP (41), MVR (53), MVP+MVR (6)
Losenno et al. [14] (2016)	Mean NYHA (3.3), STS score (15±11)	Mean NYHA (3.3), STS score (15±11)	0	TVr (12), ASD (2), ablation (2)	TVr (32), ASD (4), ablation (4), other (3)	Isolated MVR/MVP (18), MVR/ MVP±other valve±CABG (13), CABG (50), AVR/ repair±aortic±CABG (18), other (18)	Isolated MVR/MVP (62), MVR/ MVP±other valve±CABG (17), CABG (11), AVR/ repair±aortic±CABG (5), other (10)
Ghoneim et al. [15] (2016)	LVEF <30% (25%), EuroSCORE II 8.8 (3.2–30)	LVEF <30% (67%), EuroSCORE II 10.7 (1.6–19.5)	0	ASD (3), ablation (3)	Ablation (1)	12 Details not mentioned	6 Details not mentioned
Patel et al. [16] (2019)	LVEF (50%±13%), NYHA >2 (72%)	LVEF (53%±13%), NYHA >2 (56%)	NR	TVR (8), ablation (3)	TVR (21), ablation (7)	MVR (46), AVR (23), CABG (46), other (60)	MVR (63), AVR (17), CABG (32), other (75)
Zhang et al. [17] (2020)	EuroSCORE (15.3%±5.4%), NYHA >2 (66.6%)	EuroSCORE (14.8%±5.4%), NYHA >2 (64%)		TVP (8), ablation (7)	TVP (14), ablation (15)	MVP (8), MVR (8), MVR+TVP (4), MVP+TVP (4), MVR+AVR (4), CABG (2)	MVP (9), MVR (18), MVR+TVP (6), MVP+TVP (3), MVR+AVR (10), CABG (4)
Kwon et al. [18] (2022)	LVEF (59.5%±6.9%)	LVEF (57.9%±9.7%)	7	TVr/TVR (65), ASD (8), ablation (37)	TVr/TVR (97), ASD (7), ablation (39)	MVS (127), AVR (19), TVP (31), CABG (13), other (23)	MIMVS: MVS (169), AVR (30), TVP (45), CABG (13), other (25)
Monsefi et al. [19] (2022)	LVEF (56%±9%)	LVEF (52%±16%)	0	TVr (1)	TVr (7), AVR (4), TVR (7), other (1)	MVS (19), AVR (5), TVP (1), CABG (2), other (0)	MVS (27), AVR (11), TVP (2), CABG (13), other (1)
Values are presen MIMVS, minimall bypass graft; TVr, t atrial septum defe	ted as frequency or %, me y invasive mitral valve surg ricuspid repair; TVR, tricus ct repair; PFO, patent fora	an±standard deviation, gery; rRMS, redo median spid valve replacement; / men ovale; STS, Society	or median (mir sternotomy; L\ \VR, aortic valv of Thoracic Su	imum-maximum /EF, NYHA, New /e replacement; M rgeons.	ı). York Heart Association 1VP, mitral valvuloplası	; NR, not reported; MVS, mitral valv ty; MVR, mitral valve replacement;	ve surgery; CABC, coronary artery TVP, tricuspid valvuloplasty; ASD

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**Fig. 2.** Forest plot illustrating risk of mortality. CI, confidence interval; REML, restricted maximum likelihood.

				Ho	spital stay	(days)				
Study	Year	N	Treatment Mean±SD	) N	Control Mean±SD				Mean differences with 95% CI	Weight (%)
Bolotin et al. [9]	2004	38	7.1±10.26	33	11.2±7.25		4		-4.10 (8.29 to 0.09)	9.00
Kim et al. [11]	2012	22	16.3±5.6	13	19.5±17		<u> </u>		-3.20 (10.87 to 4.47)	3.52
Hiraoka et al. [12]	2013	10	18.3±8.4	27	21.5±13.2				-3.20 (12.01 to 5.61)	2.75
Ghoneim et al. [15]	2015	12	10.95±10.1	6	7.99±2.49				2.96 (5.36 to 11.28)	3.05
Vallabhajosyula et al. [13]	2015	67	11±15	220	14±12		ł		-3.00 (6.49 to 0.49)	11.32
Losenno et al. [14]	2016	40	9.06±5.38	92	13.4±9.03				-4.34 (7.35 to 1.33)	13.29
Patel et al. [16]	2019	90	7.6±5.2	90	11.7±8.3				-4.10 (6.12 to 2.08)	18.41
Monsefi et al. [19]	2022	27	16±12	53	18±11		<u> </u>		-2.00 (7.26 to 3.26)	6.52
Kwon et al. [18]	2022	162	9.06±5.23	218	17.51±15.67				-8.45 (10.96 to 5.94)	15.71
Zhang et al. [17]	2020	30	7.64±3.7	50	11.4±6.19				-3.76 (6.14 to 1.38)	16.43
Overall									-4.23 (5.77 to 2.68)	
Heterogeneity: r <sup>2</sup> =2.30, I <sup>2</sup> =	42.54	%, H <sup>2</sup>	=1.74							
Test of $\theta_i = \theta_i$ : Q(9)=14.93, p	o=0.09					-10 -5 (	0 5	10		
Test of θ=0: z=-5.37, p=0.	.00				Favors mir	imally invasive	Favors r	edo s	ternotomy	
Random-effects REMI mo	odel									

Fig. 3. Forest plot depicting length of hospital stay (days). SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

Stroke Treatment Control Risk ratio Weight Study Year No Yes No with 95% CI Yes (%) Burfeind et al. [8] 2002 6 91 7 148 1.37 (0.47-3.96) 16.46 Svensson et al. [10] 2007 6 67 163 2,281 1.23 (0.56-2.69) 24.66 Hiraoka et al. [12] 2013 9 26 2.70 (0.19-39.19) 3.36 1 1 Vallabhajosyula et al. [13] 2015 2 65 213 0.94 (0.20-4.41) 9.04 7 2015 0 12 0.18 (0.01-3.85) 2.59 Ghoneim et al. [15] 1 5 2016 2 38 90 2.30 (0.34-15.76) 6.17 Losenno et al. [14] 2 Patel et al. [16] 2019 0 90 2 88 0.20 (0.01-4.11) 2.67 Monsefi et al. [19] 2022 0 27 1 52 0.64 (0.03-15.27) 2.44 187 0.48 (0.25-0.92) 29.78 Kwon et al. [18] 2022 11 151 31 2020 6 30 47 0.24(0.01 - 4.40)2.83 Zhang et al. [17] 3 Overall 0.84 (0.51-1.39) Heterogeneity: r<sup>2</sup>=0.11, I<sup>2</sup>=17.82%, H<sup>2</sup>=1.22 Test of θ<sub>i</sub>=θ<sub>i</sub>: Q(9)=8.93, p=0.44 1/64 1/8 8 Test of 0=0: z=-0.69, p=0.49 Favors minimally invasive Favors redo sternotomy

**Fig. 4.** Forest plot illustrating risk of stroke. CI, confidence interval; REML, restricted maximum likelihood.

in the minimally invasive group and 14.13% in the sternotomy group. A pooled analysis revealed no significant difference in the risk of new-onset atrial fibrillation between the 2 surgical approaches (OR, 0.43; 95% CI, 0.14 to 1.36; p=0.15;  $I^2=47.7\%$ ) (Fig. 6B).

#### **Re-exploration for bleeding**

Ten studies, including 1,481 participants (557 for MIM-VS and 924 for redo MS), evaluated the rates of re-exploration for bleeding. The reported rate in the minimally invasive group was 4.84%, compared to 6.17% in the sternotomy group. A pooled analysis revealed no significant difference in the risk of re-exploration for bleeding between these ap-

Random-effects REML model



**Fig. 5.** Forest plot showing length of intensive care unit (ICU) stay (days). SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood.

proaches. However, a trend was observed favoring the minimally invasive approach (RR, 0.67; 95% CI, 0.44 to 1.02; p=0.06;  $I^2=0.00\%$ ) (Fig. 6C).

#### Incidence of surgical site infection

Six studies, with a total of 796 participants (264 for MIMVS and 532 for redo MS), reported on surgical site infection. The indicated infection rate was 0.39% in the minimally invasive group and 2.06% in the sternotomy group. A pooled analysis revealed no significant difference between the 2 approaches (RR, 0.54; 95% CI, 0.17 to 1.76; p=0.31;  $I^2=0.00\%$ ) (Fig. 6D).

#### Aortic cross-clamp time (in minutes)

Nine studies, involving 3438 participants (398 for MIM-VS and 3,040 for redo MS), reported on aortic cross-clamp time. No significant differences were observed between the 2 approaches (MD, -10.60; 95% CI, -27.07 to 5.86; p=0.21; I<sup>2</sup>=90.2%) (Fig. 6E).

#### Cardiopulmonary bypass time (in minutes)

Eleven studies, including 4,134 participants (663 for MIMVS and 3,471 for redo MS), provided data on cardiopulmonary bypass time. No significant differences were observed between the 2 approaches (MD, -5.10; 95% CI, -18.51 to 8.31; p=0.46; I<sup>2</sup>=83.1%) (Fig. 6F).

#### Volume of blood loss (in milliliters)

Only 2 studies, encompassing 160 participants (57 for MIMVS and 103 for redo MS), reported on blood loss. The minimally invasive approach was associated with a significant reduction in blood loss (MD, -191.61; 95% CI, -275.91 to -107.30; p<0.001;  $I^2$ =0.0%) (Fig. 6G).

#### **Publication bias**

Publication bias was assessed through the visual exam-

ination of funnel plot asymmetry and the Egger regression test, but only for outcomes including a minimum of 10 studies. Both the visual analysis and the regression test results indicated no significant risk of publication bias (Fig. 7).

## Discussion

In this systematic review and meta-analysis, our objective was to examine the current literature comparing minimally invasive surgery via a right lateral thoracotomy with redo MS for mitral valve surgery among patients who had previously undergone cardiac surgery. We aimed to identify any differences in outcomes between these approaches. The analysis indicated significant reductions in mortality, lengths of hospital stay and ICU stay, intraoperative blood loss, and new-onset AKI when the minimally invasive approach was used. Furthermore, this approach was found to be non-inferior to redo sternotomy in the rates of new-onset atrial fibrillation and stroke, re-exploration for bleeding, cardiopulmonary bypass time, and cross-clamp time.

Redo cardiac surgery is technically more challenging than primary surgery for several reasons. Surgeons must contend with dense mediastinal and pleuropericardial adhesion, the risk of injury to the functioning coronary artery bypass graft, and the de-airing of the heart. They also tend to have patients with worse baseline clinical characteristics, more comorbidities, more complex disease pathophysiology, and fewer physiological reserves [1]. In rare instances, this procedure can be associated with unique surgical complications, including annular rupture, left atrial dissection, left ventricular outflow obstruction, and Gerbode defects [20].

However, redo cardiac surgery, particularly for valvular disease, is no longer considered a predictive factor for poor outcomes. It can be performed effectively with acceptable risks when a shared decision-making process and a multidisciplinary team approach are adopted [21]. Numerous studies have reported a recent decrease in operative mortality associated with redo valve surgery via a minimally invasive approach. These studies have also reported low complication rates and promising postoperative results, making this approach a viable alternative for both primary and redo surgery [22,23]. These findings align with our meta-analysis, which indicated fewer surgery-related complications associated with the minimally invasive approach. In this review, 27 patients (4.00%) required reoperation due to bleeding, 28 patients (4.55%) developed stroke, 13 patients (3.77%) required new-onset dialysis, 13 patients (2.56%) developed new-onset atrial fibrillation, and 30 patients (4.44%) died within 30 days of the operation. The results showed no significant difference in cardiopulmonary bypass time or aortic cross-clamp time, but the general

Α				Ac	ute l	kidney injury		
		Treat	ment	Co	ntrol		Risk ratio	Weight
Study	Year	Yes	No	Yes	No		with 95% CI	(%)
Ghoneim et al. [15]	2015	1	11	1	5		0.50 (0.04-6.68)	4.83
Losenno et al. [14]	2016	0	40	6	86		0.17 (0.01-3.03)	3.99
Patel et al. [16]	2019	0	90	10	80		0.05 (0.00-0.80)	4.08
Kwon et al. [18]	2021	10	152	37	181		0.36 (0.19-0.71)	72.75
Zhang et al. [17]	2020	2	28	7	43		0.48 (0.11-2.14)	14.35
Overall						•	0.34 (0.19-0.61)	
Heterogeneity: r <sup>2</sup> =0.00, I <sup>2</sup> =0	D.00%, H	H <sup>2</sup> =1.00						
Test of $\theta_i = \theta_i$ : Q(4)=2.39, p=	0.66					1/64 1/8 1 8		
Test of 0=0: z=-3.68, p=0.0	00				Fav	ors minimally invasive Favors redo s	ternotomy	
Random-effects REML mod	del							
В				New o	onset	atrial fibrillation		
		Treat	ment	Co	ntrol		Risk ratio	Weight
Study	Year	Yes	No	Yes	No		with 95% CI	(%)
Hiraoka et al. [12]	2013	0	10	3	24		0.36 (0.02-6.48)	12.35
Vallabhaiosvula et al. [13]	2015	1	66	22	198		0.15 (0.02-1.09)	20.68
Losenno et al. [14]	2016	1	39	12	80		0.19(0.03 - 1.42)	20.42
Zhang et al. [17]	2020	11	19	18	32	<u>+</u>	1.02(0.56-1.85)	46.55
Overall	2020				02		0.43 (0.14-1.36)	10.00
Heterogeneity: $\tau^2 = 0.00 \ l^2 = 0$	0.00% F	$4^2 = 1.00$					,	
Test of $\theta = \theta$ : Q(4)=2.39, p=	0.66					1/32 1/8 1/2 2		
Test of θ=0; z=-3.68, p=0.0	00				F	avors minimally invasive Eavors redo	sternotomy	
Random-effects REML mod	del						eterneterny	
<u>^</u>					oloro	tion for blooding		
		<b>T</b>		16-67		lion of bleeding	Distantia	14/- :
Study	Voor	Vea	ment	Voo	ntrol		KISK ratio	vveight
Sludy	rear	res	INO	res	INO		WILI1 95% CI	(%)
Burfeind et al. [8]	2002	6	91	8	147		1.20 (0.43-3.35)	17.31
Kim et al. [11]	2012	0	22	2	11		0.12 (0.01-2.36)	2.08
Hiraoka et al. [12]	2013	0	10	2	25		0.51 (0.03-9.78)	2.09
Vallabhajosyula et al. [13]	2015	0	67	3	217		0.46 (0.02-8.88)	2.10
Ghoneim et al. [15]	2015	4	8	4	2		0.50 (0.19-1.33)	19.04
Losenno et al. [14]	2016	1	39	6	86		0.38 (0.05-3.08)	4.21
Patel et al. [16]	2019	2	88	2	88	<b>+</b>	1.00 (0.14-6.95)	4.87
Zhang et al. [17]	2020	1	29	4	46		0.42 (0.05-3.56)	3.98
Monsefi et al. [19]	2021	1	26	4	49		0.49 (0.06-4.18)	3.99
Kwon et al. [18]	2021	12	150	22	196		0.73 (0.37–1.44)	40.33
Overall		2				•	0.67 (0.44-1.02)	
Heterogeneity: $\tau^2=0.00$ , $\Gamma=0$	D.00%, F	1~=1.00						
Test of $\theta_i = \theta_j$ : Q(9)=3.72, p=0	0.93					1/128 1/16 1/2 4		
Test of θ=0: z=-1.85, p=0.0	)6				F	avors minimally invasive Favors redo	sternotomy	
Random-effects REML mod	del							
D						SSI		
		Treat	ment	Co	ntrol		Risk ratio	Weight
Study	Year	Yes	No	Yes	No		with 95% CI	(%)
Hiraoka et al. [12]	2013	0	10	1	26		0.85 (0.04-19.29)	14.29
Vallabhaiosvula et al. [13]	2015	0	67	1	210		1 08 (0 04-26 29)	13 71

risk of acute kidney injury requiring dialysis. (B) Forest plot depicting risk of new-onset atrial fibrillation. (C) Forest plot depicting risk of reoperation for bleeding. (D) Forest plot illustrating risk of surgical site infection (SSI). (E) Forest plot of cross-clamp time (min). (F) Forest plot of cardiopulmonary bypass time (min). (G) Forest plot illustrating volume of blood loss (mL). SD, standard deviation; CI, confidence interval; REML, restricted maximum likelihood. (Continued on next page.)

Fig. 6. (A) Forest plot illustrating

Test of  $\theta_i = \theta_j$ : Q(5)=1.15, p=0.95 Test of  $\theta = 0$ : z=-1.02, p=0.31

Heterogeneity: r<sup>2</sup>=0.00, I<sup>2</sup>=0.00%, H<sup>2</sup>=1.00

Random-effects REML model

Losenno et al. [14]

Patel et al. [16]

Zhang et al. [17]

Overall

Monsefi et al. [19]

1/64 1/8 1 8 Favors minimally invasive Favors redo sternotomy

0.32 (0.02-6.13)

0.20(0.01 - 4.11)

0.33 (0.02-6.63)

0.98 (0.09-10.35)

0.54(0.17 - 1.76)

16.13

15.27

15.46

25.14

0

0 90

0 30

1

40

26

2016

2019

2020

2022

3

2 88

2 48

2 51

89

E			A	ortic	cross clan	np time (min)		
		Т	reatment	С	ontrol		Mean differences	Weight
Study	Year	N	Mean±SD	N	Mean±SD		with 95% CI	(%)
Svensson et al. [10]	2007	80	57±37	2,444	94±41 -	<b>-</b>	-37.00 (-46.10 to -27.90)	18.41
Kim et al. [11]	2012	22	91.3±26.7	13	101.9±56		-10.60 (-37.97 to 16.77)	12.67
Vallabhajosyula et al. [13]	2015	67	104±38	220	130±71		-26.00 (-43.74 to -8.26)	15.91
Losenno et al. [14]	2016	40	123±37	92	105±46		-18.00 (1.85 to 34.15)	16.43
Monsefi et al. [19]	2022	27	52±26	53	48±22		-4.00 (-6.85 to 14.85)	17.99
Kwon et al. [18]	2022	162	88.3±37.9	218	99±42.7		-10.70 (-18.98 to -2.42)	18.59
Heterogeneity: 7 <sup>2</sup> =361.49	1 <sup>2</sup> =00	16%	$H^2 = 10.16$				10.00 ( 27.07 to 3.80)	
Test of $A = A \cdot O(5) = 52.50$	n=0.00	יייי. ו	, 11 - 10.10		_	40 20 0 20	10	
Test of $\theta_i = 0_j$ . $Q(0) = 32.50$ ,	p=0.00	,			-	40 -20 0 20	- 40	
Random-effects REML m	odel				Favo	s minimally invasive	-avors redo sternotomy	
	ouo.		0					
F			Card	iopuli	monary by	pass time (min)		
o	V		Treatment		Control	_	Mean differences	Weight
Study	rear	IN	Mean±5L	יו (	Mean±Si		with 95% CI	(%)
Burfeind et al. [8]	2002	97	188.9±72.9	9 155	5 157±53			10.14
Bolotin et al. [9]	2004	38	160±64	33	157±53.9		3.00 (-24.76 to 30.76)	7.81
Svensson et al. [10]	2007	80	123±43	2,444	132±58		-9.00 (-21.82 to 3.82)	10.61
Kim et al. [11]	2012	22	170.6±46.8	3 13	209.9±102.	9	-39.30 (-88.95 to 10.35)	4.50
Hiraoka et al. [12]	2013	10	145±25	27	135±28	-+=	— 10.00 (-9.78 to 29.78)	9.36
Vallabhajosyula et al. [13]	2015	67	153±42	220	172±83		-19.00 (-39.65 to 1.65)	9.19
Losenno et al. [14]	2016	40	201±63	92	180±75	+-	21.00 (-5.58 to 47.58)	8.04
Monsefi et al. [19]	2022	27	101±39	53	92±45		— 9.00 (-10.97 to 28.97)	9.32
Kwon et al. [18]	2022	162	172.6±59.9	9 218	183±86.3		-10.40 (-25.89 to 5.09)	10.15
Zhang et al. [17]	2022	30	130.2±19.3	3 50	165.2±27.6		-35.00 (-46.24 to -23.76	) 10.85
Patel et al. [16]	2019	90	144±53.6	6 166	171±67.2		-27.00 (-43.10 to -10.90	) 10.04
Overall							-5.10 (-18.51 to 8.31)	
Heterogeneity: r <sup>2</sup> =398.65	, I <sup>2</sup> =83	.05%	, H <sup>2</sup> =5.90					
Test of θ <sub>i</sub> =θ <sub>i</sub> : Q(10)=66.44	, p=0.0	00			-	-100 -50 0	50	
Test of 0=0: z=-0.75, p=0	).46				Favors	minimally invasive Fa	avors redo sternotomv	
Random-effects REML me	odel					,		
G					Blood loss	s (mL)		
-	т.	·oatr	ont	Contro	1		Mean differences	Woight
Study Year	• N	Mea	an±SD N	Mear	n±SD		with 95% CI	(%)
Monsefi et al. [19] 2022	27	56	6±359 53	793	±410		-227.00 (-409.46 to -44.54)	21.35
Zhang et al. [17] 2022	30	51	5±188 50	697	±222		-182.00 (-277.05 to -86.95)	78.65
Overall							-191.61 (-275.91 to -107.30)	

Overall Heterogeneity:  $\tau^2$ =0.00, I<sup>2</sup>=0.00%, H<sup>2</sup>=0.00 Test of θ<sub>i</sub>=θ<sub>i</sub>: Q(1)=0.18, p=0.67 Test of 0=0: z=-4.45, p=0.00 Random-effects REML model

-400 -300 -200 -100 0 Favors minimally invasive Favors redo sternotomy

Fig. 6. (Continued; caption shown on previous page).

trend favored minimally invasive surgery. This reflects the growing expertise in cannulation methods and improvements in surgical technique. While some studies have reported an increased incidence of stroke with MIMVS, our analysis did not indicate this [24,25]. This discrepancy could be attributed to the cardiopulmonary bypass approaches used. Specifically, retrograde arterial perfusion and cold fibrillatory arrest without an aortic cross-clamp have been associated with a higher incidence of stroke [25].

Numerous indications for reoperation exist, but unfortunately, these were not extensively reported in the included studies. Typically, reoperation can be attributed to factors such as structural valvular degeneration, nonstructural dysfunction, valve thrombosis, paravalvular leak, prosthetic valve endocarditis, and recurrent rheumatic disease [2]. Several perioperative factors influencing in-hospital mortality have been identified. Our analysis revealed that the operative approach was consequential in determining mortality. The MIMVS approach reduced the risk of mortality by almost 50%. However, most studies, except for those by Patel et al. [16] and Losenno et al. [14], did not control for confounding variables. It is plausible that mortality rates could have been similarly influenced by various baseline demographic and clinical variables, as well as pre-existing comorbidities. Some studies have suggested that early mortality is associated with factors such as advanced age, female sex, advanced New York Heart Functional Association class, lower ejection fraction, emergent or urgent surgery, concomitant procedures, and history of myocardial infarction [3,26].

For patients with degenerated mitral bioprostheses deemed inoperable or at high surgical risk, valve-in-valve transcatheter mitral valve replacement (ViV-TMVR) may serve as an alternative to conventional redo surgery. However, data are lacking regarding its long-term durability. A recent meta-analysis comparing ViV-TMVR to redo surgi-



Fig. 7. Funnel plot reflecting assessment of publication bias. (A) Bleeding. (B) Cardiopulmonary bypass time. (C) Hospital stay. (D) Mortality. (E) Stroke. CI, confidence interval.

cal mitral valve replacement has revealed promising results. ViV-TMVR has been associated with a significant reduction in procedural complications, such as stroke, bleeding, AKI, arrhythmias, and permanent pacemaker insertion. It has also been linked to shorter hospital stays, with no significant difference in mortality rates [27]. Transcatheter options are an evolving field and have not yet become the established standard of care. However, they hold the potential for more frequent use in the future. Currently, the data are insufficient to compare the outcomes of ViV-TMVR and minimally invasive mitral valve surgery, indicating a need for further research.

The primary limitation of this study pertains to the retrospective, non-randomized nature of the underlying studies. Despite efforts to eliminate bias, several biases inherent to retrospective cohort studies persist. These studies carry an elevated risk of selection bias because individuals are selected after the outcome has occurred. The use of unplanned or less rigorous data collection methods, or the absence of a priori reporting of the analysis plan and protocol, can lead to information bias. Furthermore, the retrospective comparative studies did not include long-term follow-up. Second, multiple confounding factors were not measured or adjusted in the results due to the absence of relevant details from the original studies. Unacknowledged or poorly measured confounders can undermine the association being inferred. As is the case with most meta-analyses of observational studies, it is not possible to establish causal effects from the results. Third, no information was presented on patient-centered reported outcomes such as health status, pain, patient satisfaction, and quality of life. The importance of patient-centered outcomes is increasingly recognized in healthcare research, as these measures reflect clinically relevant issues that are particularly meaningful to patients. Fourth, the surgical approach was determined based on the surgeon's preference. Given the steep learning curve associated with the minimally invasive approach, it is expected that surgery times and outcomes will improve as experience is gained. Differences in surgeon skill set and expertise can introduce bias for or against the minimally invasive approach. The true benefits of this approach are more likely to be fully realized in high-volume centers.

## Conclusion

The existing data, which are limited to retrospective comparisons of small cohorts undergoing MIMVS versus

redo MS for mitral valve surgery in patients with previous cardiac surgery, do not provide information on outcomes after hospital discharge. Current evidence from 12 studies suggests that MIMVS is associated with decreased mortality, shorter hospital and ICU stays, less blood loss during surgery, and a lower incidence of new-onset AKI requiring dialysis. To eliminate biases and validate our findings, large-scale randomized control trials are necessary. Additionally, more data are required on durability and long-term outcomes.

## **Article information**

## ORCID

Muhammad Ali Tariq: https://orcid.org/0000-0003-1108-0731 Minhail Khalid Malik: https://orcid.org/0000-0002-3823-2670 Qazi Shurjeel Uddin: https://orcid.org/0000-0003-4850-2125 Zahabia Altaf: https://orcid.org/0000-0003-3638-2277 Mariam Zafar: https://orcid.org/0000-0003-4985-0009

## Author contributions

Conceptualization: MAT. Data curation: QSU, ZA, MZ. Formal analysis: MAT, MKM. Writing-original draft: MKM, QSU, ZA, MZ. Writing-review & editing: MAT, MKM. Final approval of the manuscript: all authors.

## Conflict of interest

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